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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/728,041	12/01/2000	Irene Teresa Rombel	UTSD:679US/GNS	2581

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Gina N. Shishima
FULBRIGHT & JAWORSKI L.L.P.
Suite 2400
600 Congress Avenue
Austin, TX 78701

EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/728,041	Applicant(s) ROMBEL ET AL.	
	Examiner Jeffrey Fredman	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-90* is/are pending in the application.

4a) Of the above claim(s) *4,8,9,14-19 and 26-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-7,10-13,20-25 and 90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-25 and 90, and species Trypansoma cruzi and GFP in Paper No. 13 is acknowledged.

2. Claims 4, 8, 9, 14-19 are drawn to nonelected species and are therefore withdrawn from consideration.

3. Claims 26-89 are drawn to nonelected groups and are therefore withdrawn from consideration.

Specification

4. The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 94, lines 11-12, for example. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-3, 11-13, 20 and 22-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Hawke et al (Biotechniques (1997) 23(4):619-621).

Hawke teaches an ORF selection vector (see figure 1) comprising:

(a) a promoter (Hawke teaches the use of the pLac promoter in figure 1)

(b) a start codon operably linked to the promoter (Hawke teaches the use of the LacZ start codon which is operably linked to the pLac promoter, see figure 1),

(c) a Green Fluorescent Protein reporter gene that is positioned downstream from the promoter and start codon and that is out of frame (Hawke states in the figure legend of figure 1 that "The vector sequence shows the oligonucleotide linker (boxed), termination codon (reverse image) and out-of-frame GFPuv coding sequence"(see figure 1, legend).

Hawke teaches insertion of part of an ORF of a nucleic acid from the genomic DNA of m13 to place the reporter gene into frame (see page 620, column 3).

The GFP of Hawke lacks a start codon (See figure 1).

Hawke teaches the inclusion of restriction sites between the start codon and the reporter gene, such as HindIII and XbaI (see figure 1, panel A).

Hawke teaches inclusion of the pUC 19 origin of replication into the vector (see figure 1).

Hawke teaches inclusion of an Ampicillin selectable marker which is in frame and expressed in the host cell (see figure 1).

7. Claims 1-3, 11-13, 20, 22-25 and 90 are rejected under 35 U.S.C. 102(e) as being anticipated by Litman et al (U.S. Patent 6,284,496).

Litman teaches an ORF selection vector (see figure 1) comprising:

(a) a promoter (Litman teaches the use of the pLac promoter in figure 1)

(b) a start codon operably linked to the promoter (Litman teaches the use of the LacZ start codon which is operably linked to the pLac promoter, see figure 1),

(c) a Green Fluorescent Protein reporter gene that is positioned downstream from the promoter and start codon and that is out of frame (Litman states regarding figure 1 that "the engineered indicator sequence and restriction sites creating an out-of-frame sequence (see column 3, lines 32-34)".

Litman teaches insertion of part of an ORF of a nucleic acid from the genomic DNA of m13 to place the reporter gene into frame (see column 7, lines 47-67 and column 4).

The GFP of Litman lacks a start codon (See figure 1).

Litman teaches the inclusion of restriction sites between the start codon and the reporter gene, such as HindIII and XbaI (see figure 1).

Litman teaches inclusion of the pUC 19 origin of replication into the vector (see figure 1).

Litman teaches inclusion of an Ampicillin selectable marker which is in frame and expressed in the host cell (see figure 1).

Litman further teaches an expression construct lacking the reporter gene (see column 4, line 2).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 5-7 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hawke as applied to claims 1-3, 11-13, 20 and 22-25 and further in view of Schonek et al (Eur. J. Biochem. (1997) 243:739-747).

Hawke teaches an ORF selection vector (see figure 1) comprising:

(a) a promoter (Hawke teaches the use of the pLac promoter in figure 1)

(b) a start codon operably linked to the promoter (Hawke teaches the use of the LacZ start codon which is operably linked to the pLac promoter, see figure 1),

(c) a Green Fluorescent Protein reporter gene that is positioned downstream from the promoter and start codon and that is out of frame (Hawke states in the figure

legend of figure 1 that "The vector sequence shows the oligonucleotide linker (boxed), termination codon (reverse image) and out-of-frame GFPuv coding sequence"(see figure 1, legend).

Hawke teaches insertion of part of an ORF of a nucleic acid from the genomic DNA of m13 to place the reporter gene into frame (see page 620, column 3).

The GFP of Hawke lacks a start codon (See figure 1).

Hawke teaches the inclusion of restriction sites between the start codon and the reporter gene, such as HindIII and XbaI (see figure 1, panel A).

Hawke teaches inclusion of the pUC 19 origin of replication into the vector (see figure 1).

Hawke teaches inclusion of an Ampicillin selectable marker which is in frame and expressed in the host cell (see figure 1).

Hawke does not teach the use of Trypanosoma cruzi open reading frame sequences.

Schonek teaches analysis of Trypanosoma cruzi open reading frame sequences (see abstract and pages 739-740).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to screen Trypanosoma cruzi open reading frame sequences using the method of Hawke since Hawke states "To facilitate identification of amplification products containing open reading frames, we have engineered a vector, pGFPfs, that affords positive selection of recombinants based upon the continuity of coding sequencine within a lacZ:insert:GFP (Green fluorescent protein) fusion construct

that is expressed in E. coli (page 619, column 1)". So Hawke motivates the use of the vector to identify open reading frames, including frames beginning at the 5' end of the coding region. Schonek teaches abundant motivation for isolation of Trypansoma cruzi open reading frames, including 5' ends (see page 742, column 1) and expressly motivates cloning Trypansoma cruzi genes such as LipDH since these genes may be "attractive target molecule for a structure based design of new antitrypansomal drugs (see page 245, column 2)". An ordinary practitioner would have been motivated to screen Trypanosoma cruzi genomic sequence for open reading frames in order to identify targets which could be possible drug targets in order to treat Chagas disease, caused by Trypanosoma cruzi (see Schonek, page 739, column 2).

11. Claims 5-7 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Litman et al (U.S. Patent 6,284,496) as applied to claims 1-3, 11-13, 20, 22-25 and 90 and further in view of Schonek et al (Eur. J. Biochem. (1997) 243:739-747).

Litman teaches an ORF selection vector (see figure 1) comprising:

(a) a promoter (Litman teaches the use of the pLac promoter in figure 1)

(b) a start codon operably linked to the promoter (Litman teaches the use of the LacZ start codon which is operably linked to the pLac promoter, see figure 1),

(c) a Green Fluorescent Protein reporter gene that is positioned downstream from the promoter and start codon and that is out of frame (Litman states regarding figure 1 that "the engineered indicator sequence and restriction sites creating an out-of-frame sequence (see column 3, lines 32-34)".

Litman teaches insertion of part of an ORF of a nucleic acid from the genomic DNA of m13 to place the reporter gene into frame (see column 7, lines 47-67 and column 4).

The GFP of Litman lacks a start codon (See figure 1).

Litman teaches the inclusion of restriction sites between the start codon and the reporter gene, such as HindIII and XbaI (see figure 1).

Litman teaches inclusion of the pUC 19 origin of replication into the vector (see figure 1).

Litman teaches inclusion of an Ampicillin selectable marker which is in frame and expressed in the host cell (see figure 1).

Litman further teaches an expression construct lacking the reporter gene (see column 4, line 2).

Litman does not teach the use of Trypanosoma cruzi open reading frame sequences.

Schonek teaches analysis of Trypanosoma cruzi open reading frame sequences (see abstract and pages 739-740).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to screen Trypanosoma cruzi open reading frame sequences using the method of Litman since Litman states "The present invention provides a DNA expression vector for positively selecting out-of-reading-frame mutations including frameshifts and stop codons in DNA sequences which need to be tested for frameshifts and/or stop codons. The vector is engineered to include a

promotor operatively linked to an expressible reporter gene through a linkage sequence. The linkage sequence includes at least two restriction sites and an engineered frameshift (column 3, lines 40-47)". So Litman motivates the use of the vector to identify open reading frames, including frames beginning at the 5' end of the coding region. Schonek teaches abundant motivation for isolation of Trypansoma cruzi open reading frames, including 5' ends (see page 742, column 1) and expressly motivates cloning Trypansoma cruzi genes such as LipDH since these genes may be "attractive target molecule for a structure based design of new antitrypansomal drugs (see page 245, column 2)". An ordinary practitioner would have been motivated to screen Trypanosoma cruzi genomic sequence for open reading frames in order to identify open reading frames which will serve as targets for drugs that could be used in order to treat Chagas disease, caused by Trypanosoma cruzi (see Schonek, page 739, column 2).

12. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hawke as applied to claims 1-3, 11-13, 20 and 22-25 and further in view of Hernan et al (Biochemistry (1992) 31:8619-8628).

Hawke teaches an ORF selection vector (see figure 1) comprising:

(a) a promoter (Hawke teaches the use of the pLac promoter in figure 1)

(b) a start codon operably linked to the promoter (Hawke teaches the use of the LacZ start codon which is operably linked to the pLac promoter, see figure 1),

(c) a Green Fluorescent Protein reporter gene that is positioned downstream from the promoter and start codon and that is out of frame (Hawke states in the figure legend of figure 1 that "The vector sequence shows the oligonucleotide linker (boxed),

termination codon (reverse image) and out-of-frame GFPuv coding sequence"(see figure 1, legend).

Hawke teaches insertion of part of an ORF of a nucleic acid from the genomic DNA of m13 to place the reporter gene into frame (see page 620, column 3).

The GFP of Hawke lacks a start codon (See figure 1).

Hawke teaches the inclusion of restriction sites between the start codon and the reporter gene, such as HindIII and XbaI (see figure 1, panel A).

Hawke teaches inclusion of the pUC 19 origin of replication into the vector (see figure 1).

Hawke teaches inclusion of an Ampicillin selectable marker which is in frame and expressed in the host cell (see figure 1).

Hawke does not teach the use of the T7 promoter.

Hernan teaches the use of the T7 promoter in expression vectors (see page 8625, columns 1 and 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the vector of Hawke to replace the lac promoter with the T7 promoter taught by Hernan since Hernan states "The T7 promoter is among the strongest promoters in E. coli and generally results in rates of transcription 5-10 fold greater than that obtainable with the lac or tac promoter (see page 8625, column 2)". An ordinary practitioner would have been motivated to substitute the T7 promoter of Hernan into the vector of Hawke in order to increase the yield and consequent

sensitivity of the assay by 5-10 fold, due to the improved transcription available by the T7 promoter.

13. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Litman et al (U.S. Patent 6,284,496) as applied to claims 1-3, 11-13, 20, 22-25 and 90 and further in view of Hernan et al (Biochemistry (1992) 31:8619-8628).

14. Litman teaches an ORF selection vector (see figure 1) comprising:

(a) a promoter (Litman teaches the use of the pLac promoter in figure 1)

(b) a start codon operably linked to the promoter (Litman teaches the use of the LacZ start codon which is operably linked to the pLac promoter, see figure 1),

(c) a Green Fluorescent Protein reporter gene that is positioned downstream from the promoter and start codon and that is out of frame (Litman states regarding figure 1 that "the engineered indicator sequence and restriction sites creating an out-of-frame sequence (see column 3, lines 32-34)".

Litman teaches insertion of part of an ORF of a nucleic acid from the genomic DNA of m13 to place the reporter gene into frame (see column 7, lines 47-67 and column 4).

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Litman teaches inclusion of an Ampicillin selectable marker which is in frame and expressed in the host cell (see figure 1).

Litman further teaches an expression construct lacking the reporter gene (see column 4, line 2).

Litman does not teach the use of the T7 promoter.

Hernan teaches the use of the T7 promoter in expression vectors (see page 8625, columns 1 and 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the vector of Litman to replace the lac promoter with the T7 promoter taught by Hernan since Hernan states "The T7 promoter is among the strongest promoters in E. coli and generally results in rates of transcription 5-10 fold greater than that obtainable with the lac or tac promoter (see page 8625, column 2)". An ordinary practitioner would have been motivated to substitute the T7 promoter of Hernan into the vector of Litman in order to increase the yield and consequent sensitivity of the assay by 5-10 fold, due to the improved transcription available by the T7 promoter.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers

for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1637

December 17, 2002